CLAIMS:

1.   A method for identifying a test agent as reducing the level of differentiation of T cells into Th1 cells comprising reducing MEKK1 catalytic activity in said T cells.

2.   The method of Claim 1, wherein reducing of said MEKK1 catalytic activity comprises increasing the level of differentiation of said T cells into Th2 cells.

3.   The method of Claim 1, wherein the reducing of said MEKK1 catalytic activity comprises increasing the level of one or more Th2 cell cytokine that is produced by said T cells.

4.   The method of Claim 3, wherein the increased level of said Th2 cytokine occurs in the absence of an increase in the level of one or more Th1 cytokine.

5.   The method of Claim 4, wherein said Th1 cytokine is chosen from one or more of interferon-gamma and Interleukin-2.

6.   The method of Claim 3, wherein said Th2 cytokine is chosen from one or more of Interleukin-4, Interleukin-5, Interleukin-10, and Interleukin-13.

7.   The method of Claim 3, wherein said increasing the level of said Th2 cell cytokine comprises increasing the level of mRNA encoding said Th2 cytokine.

8.   The method of Claim 7, wherein said mRNA encoding said Th2 cytokine is increased 5 fold.

9.   The method of Claim 3, wherein said reducing of said MEKK1 catalytic activity comprises increasing the level of proliferation of Th2 cells that differentiate from said T cells.

10.   The method of Claim 3, wherein said reducing of said MEKK1 catalytic activity comprises introducing a mutation in the gene encoding MEKK1.

11.   The methods of Claim 3, wherein said T cells comprise thymocyte cells.

12.   The methods of Claim 3, wherein said T cells comprise splenocyte cells.

13.   The methods of Claim 3, wherein said T cells are *in vitro*.

14.   The methods of Claim 13, wherein said T cells are *in vivo* in an animal.

15.   The methods of Claim 14, wherein said animal is human.

16.   The method of Claim 15, wherein said human is chosen from one or more of a human that is:

      (a)   suspected of having a Th1-mediated disease;

      (b)   not suspected of having a Th1-mediated disease;

      (c)   suspected of being capable of developing a Th1-mediated disease; and

      (d)   suspected of not being capable of developing a Th1-mediated disease.

17.   The methods of Claim 16, wherein said Th1-mediated disease is chosen from multiple sclerosis, type 1 diabetes, autoimmune thyroiditis, and rheumatoid arthritis.

18.   A method for identifying a test agent as reducing the level of differentiation of T cells into Th1 cells, comprising:

      (a)   providing:

            i)   a test agent; and

            ii)   MEKK1; and

      (b)   contacting said test agent and said MEKK1; and

      (c)   detecting reduced MEKK1 kinase activity in the presence of said agent compared to in the absence of said agent, thereby identifying said test agent as causing one or more of increasing Th2 cells, decreasing the level of Th1 cells, and decreasing Th1 disease.

19.   The method of Claim 16, wherein said method comprises one or more of:

(a)   identifying said agent as increasing the level of differentiation of said T cells into Th2 cells;

(b)   identifying said agent as increasing the level of one or more Th2 cell cytokine that is produced by said T cell; and

(c)   identifying said agent as increasing the level of proliferation of Th2 cells that differentiate from said T cells.

20.   A method for increasing Th2 cytokine levels produced by T cells, comprising:

(a)   providing:

(i)   an inhibitor of ITCH;

(ii)   T cells; and

(iii)   test agent; and

(b)   contacting said T cells in the presence of said test agent to produce contacted T cells and in the absence of said test agent to produce control T cells; and

(c)   detecting reduced activity of ITCH in said contacted T cells compared to ITCH in said control T cells, wherein said detecting identifies said test agent as increasing Th2 cytokine levels produced by T cells.

21.   A method for increasing Th2 cytokine levels produced by T cells, comprising:

(a)   providing:

(i)   a kinase inhibitor, wherein said kinase is one or more of MEKK1 and JNK1;

(ii)   T cells;

(iii)   test agent; and

(b)   contacting said T cells in the presence of said test agent to produce contacted T cells and in the absence of said test agent to produce control T cells; and

(c)   detecting reduced activity of said kinase in said contacted T cells compared to said kinase in said control T cells, wherein said detecting identifies said test agent as increasing Th2 cytokine levels produced by T cells.

22.   The methods of Claim 20 and Claim 21, further comprising, (d) identifying said test agent as increasing the level of one or more of Th2 cytokine.

23.   The methods of Claim 22, wherein said Th2 cytokine is one or more of Interleukin-4, Interleukin-5, Interleukin-10, and Interleukin-13.

24.   The methods of Claim 20 and Claim 21, further comprising, (d) identifying said test agent as decreasing the level of Th1 cytokines.

25.   The method of Claim 21, wherein said kinase inhibitor comprises SB600125.

26.   A method for increasing Th2 cytokine levels produced by T cells, comprising reducing the activity of an ITCH.

27.   A method for increasing Th2 cytokine levels produced by T cells, comprising reducing the activity of a MEKK1.

28.   A method for increasing Th2 cytokine levels produced by T cells, comprising reducing the activity of a JNK1.

29.   A method for increasing Th2 cytokine levels produced by T cells, comprising:
    (a)   providing:
        (i)   T cells; and
        (ii)   agent that reduces activity of an ITCH; and
    (b)   contacting said T cells with said agent under conditions such that said agent reduces said activity of said ITCH.

30.   A method for increasing Th2 cytokine levels produced by T cells, comprising:
    (a)   providing:
        (i)   T cells; and
        (ii)   agent that reduces activity of a kinase, wherein said kinase is one or more of MEKK1 and JNK 1; and
    (b)   contacting said T cells with said agent and without said agent under conditions such that said agent reduces activity of said kinase.

31.   The method of Claim 29 and 30, further comprising (c) identifying said test agent as comprising increasing the level of Interleukin-10 produced by said T cells.

32.   The method of Claim 29 and 30, wherein said T cells are inflammatory disease T cells.

23.   The method of Claim 32, wherein said inflammatory disease is one or more of type 1 diabetes, autoimmune thyroiditis, multiple sclerosis and rheumatoid arthritis.

34.   A method for increasing Th2 cytokine levels produced by pro-inflammatory disease T cells, comprising:

(a)   providing:

(i)   pro-inflammatory disease T cells; and

(ii)   agent that reduces activity of an ITCH; and

(b)   contacting said pro-inflammatory disease T cells with said agent under conditions such that said agent increases the level of Interleukin-10 produced by said T cells.

35.   A method for reducing inflammation and disease associated with Th1 cell abundance by increasing the *in vivo* production of Th2 cells comprising reducing one or more of MEKK1-MEKK4/MKK7-JNK-ITCH cascade pathway activity and direct MEKK1-ITCH protein to protein interactions.

36.   The method of Claim 35, wherein said reducing is comprises using one or more MEKK1 enzyme inhibitors.

37.   The method of Claim 36, wherein said enzyme inhibitors comprises SP600125.

38.   The method of Claim 35, wherein said reducing comprises using one or more neutralizing antibodies that specifically bind to MEKK1.

39.   The method of Claim 35, wherein said reducing is achieved by reducing expression of the MEKK1 gene.

40.   The method of Claim 35, wherein said reducing comprises using one or more MEKK4/MKK7 enzyme inhibitors.

41.   The method of Claim 40, wherein said MEKK4/MKK7 enzyme inhibitors comprises SP600125.

42.   The method of Claim 35, wherein said reducing comprises neutralizing antibodies that specifically bind to MEKK4/MKK7.

43.   The method of Claim 35, wherein said reducing is comprises inhibiting expression of the MEKK4/MKK7 gene.

44.   The method of Claim 35, wherein said reducing comprises using ITCH enzyme inhibitors.

45.   The method of Claim 35, wherein said reducing comprises using neutralizing antibodies that specifically bind to ITCH.

46.   The method of Claim 35, wherein said reducing comprises inhibiting the expression of the ITCH gene.

47.   The method of Claim 35, wherein said inhibitor comprises SP600125.

48.   The method of Claim 37, wherein the expression of a JNK gene is suppressed by the use of one or more of RNAi, and antisense molecules.

49.   The method of Claim 37, wherein the expression of said MEKK1 gene is suppressed by the use of one or more of RNAi and antisense molecules.

50.   The method of Claim 37, wherein the expression of the MEKK4/MKK7 gene is suppressed by the use of one or more of RNAi and antisense molecules.

51.   The method of Claim 37, wherein the expression of the ITCH gene is suppressed by the use of one or more of RNAi and antisense molecules.

52.   The method of Claim 37, wherein the neutralizing antibody is chosen from human antibody and humanized antibody that invoke minimum and therapeutically acceptable level of immunogenic defense response in a human.

53.   The method of Claim 37, wherein the MEKK1-ITCH interactions are reduced by using SP600125.

54.   The method of Claim 35, wherein MEKK1-ITCH interactions are reduced by the use of neutralizing antibodies against one or more of MEKK1 and ITCH.

55.   The method of Claim 43, wherein the neutralizing antibody is chosen from human antibody and humanized antibody that invoke minimum and therapeutically acceptable level of immunogenic defense response in a human.

56.   A composition comprising a transgenic mouse that comprises $MEKK1^-/MEKK1^-$ or $MEKK1^-/MEKK1^+$.

57.   A method for identifying therapeutic agents that are useful in reducing one or more of MEKK -MEKK4/MKK7- JNK-ITCH cascade pathway activity and direct MEKK1-ITCH protein to protein interactions comprising:
>   (a)   providing;
>   >   (i)   WT and $MEKK1^{KD}$ thymocytes stimulated with;
>   >   (ii)   anti-CD3;
>   >   (iii)   anti-CD28 for 24 hrs; and
>   >   (iv)   in the absence or presence (0.5 mM) of a JNK inhibitor;
>   (b)   preparing cell lysates from said thymocytes;
>   (c)   immunoblotting said lysates; and
>   (d)   determining levels of one or more of ITCH, c-Jun and JunB to identify therapeutic agents that are useful in reducing cascade pathway activity.

58.   A method for reducing inflammation and disease associated with Th1 cell abundance by increasing the *in vivo* production of Th2 cells.

59.   A method wherein said JNK inhibitor comprises SP600125.

60.   A method for reducing inflammation and disease associated with Th1 cell abundance by increasing the *in vivo* production of Th2 cells wherein said disease is chosen from multiple sclerosis, type 1 diabetes, autoimmune thyroiditis, and rheumatoid arthritis.

61.   A method for reducing the symptoms of type 1 diabetes by increasing *in vivo* production of Th2 cells comprising reducing one or more of MEKK1-MEKK4/MKK7-JNK-ITCH cascade pathway activity and direct MEKK1-ITCH protein to protein interactions.

62.   A method for reducing the symptoms of autoimmune thyroiditis by increasing *in vivo* production of Th2 cells comprising reducing one or more of MEKK1-MEKK4/MKK7-JNK-ITCH cascade pathway activity and direct MEKK1-ITCH protein to protein interactions.

63.   A method for reducing the symptoms of multiple sclerosis by increasing *in vivo* production of Th2 cells comprising reducing one or more of MEKK1-MEKK4/MKK7-JNK-ITCH cascade pathway activity and direct MEKK1-ITCH protein to protein interactions.